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Application of recurrent laryngeal nerve monitoring technology in thyroid and parathyroid surgery

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Highlights

- A systematic introduction to the electrophysiological principles of recurrent laryngeal nerve (RLN) monitoring, the principles of RLN monitoring equipment, and the main RLN monitoring devices currently available.
- A discussion of the standardized procedures for RLN monitoring, along with methods for managing abnormal conditions during surgery.
- An analysis of the development status and future prospects of RLN monitoring technology.

Abstract

Protecting the recurrent laryngeal nerve (RLN) and superior laryngeal nerve during thyroid and parathyroid surgery remains a significant challenge. Traditional methods primarily rely on visual identification and regional protection techniques to minimize nerve injury. However, these approaches often face challenges such as limited working space, high procedural difficulty, and incomplete tissue removal. Intraoperative nerve monitoring uses neurophysiological techniques to assess the functional integrity of nerves, aiming to prevent or reduce nerve damage. Intraoperative nerve monitoring for laryngeal nerve protection during thyroid and parathyroid surgery provides an effective means of evaluating RLN damage. For successful RLN monitoring, both monitoring personnel and surgeons need a solid understanding of nerve monitoring principles, follow of standardized surgical procedures, and be able to troubleshoot abnormal signals during surgery. With ongoing advancements in technology, nerve monitoring devices are expected to become more sensitive, offering rapid and precise waveform analysis, and enhancing user-friendliness. Additionally, minimally invasive thyroidectomy and robot-assisted surgical systems hold promising potential for the future of thyroid surgery. This paper reviews the use of Intraoperative nerve monitoring and RLN monitoring, incorporating the latest research from both domestic and international studies. It discusses the importance of RLN monitoring, the principles of monitoring technologies, current research on RLN monitoring technology, guidelines for nerve monitoring, and strategies for managing and analyzing abnormal monitoring signals.

Keywords: Intraoperative nerve monitoring, recurrent laryngeal nerve, thyroid

Introduction

Thyroid cancer has become one of the fastest-growing solid malignancies worldwide, with rising incidence and prevalence. According to a 2013 analysis of data from 255 cancer registries conducted by the National Cancer Registry Center, thyroid cancer ranks as the seventh most common cancer overall and the fifth most common among women with a significant upward trend in its incidence [1]. Recurrent laryngeal nerve (RLN) injury remains one of the most common and serious complications associated with thyroidectomy. Several factors contribute to RLN injury, including age, differentiated thyroid carcinoma, and skin color. The overall incidence of RLN injury within 30 days following thyroid surgery is reported to be 6.0% [2]. RLN injury is widely recognized as a major complication of thyroid surgery. In China, the incidence of intraoperative RLN injury ranges from 2.23% to 7.40% [3].

Intraoperative neurophysiological monitoring

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(IONM) applies electrophysiological principles to assess nerve function through electrical stimulation, which induces nerve impulses that travel along the monitored nerve, triggering muscle contractions and generating electromyography (EMG) signals [4]. The advantages of IONM include enhanced nerve identification and the prevention of nerve injury. IONM is particularly valuable in protecting motor nerves during thyroid and parathyroid surgeries, especially in high-risk procedures involving nerve damage, minimally invasive laparoscopic surgeries with limited working space, and surgeries where vocal function preservation is critical [5, 6].

Although RLN monitoring offers numerous technical advantages, its effectiveness depends on proper implementation. Surgical staff must undergo specialized training in laryngeal nerve recording to ensure accurate functional assessment and provide effective assistance to the surgeon. This article aims to introduce key aspects of RLN monitoring in thyroid surgery to help clinicians better understand, standardize, and appropriately apply RLN monitoring technology in clinical practice.

Significance of RLN monitoring

Protecting the RLN has always been a key focus in thyroid surgery. Since the late 19th century, surgeons have employed various anatomical techniques to safeguard the RLN, requiring meticulous dissection and leaving a portion of thyroid tissue to protect the nerve. These techniques include the “nerve palpation protection technique” and the “anatomical exposure technique.” The nerve palpation technique involves gently identifying and isolating the RLN through tactile exploration during surgery, while the anatomical exposure technique requires detailed dissection to directly visualize and protect the nerve. Both approaches aim to minimize the risk of RLN injury during thyroidectomy, which is essential for preserving vocal function and preventing postoperative complications. However, incomplete removal of surrounding tissues poses a risk of requiring multiple surgeries to excise tumors, which in turn increases the likelihood of RLN injury.

In 1966 and 1970, Shedd and Flisberg independently proposed the use of nerve monitoring technology during thyroid surgery to help surgeons assess RLN function and detect potential damage during procedures [7, 8]. Since then, RLN monitoring has gained increasing attention from surgeons.

The RLN is a branch of the vagus nerve that emerges after the nerve enters the thoracic cavity. The terminal branches of the RLN innervate the mucosa below the glottis and all laryngeal muscles except the cricothyroid muscle, making it the primary motor nerve for these muscles. Clinically, unilateral RLN injury can result in unilateral vocal cord paralysis, while bilateral RLN damage may lead to aphonia, respiratory distress, and even suffocation [9].

In addition, a rare anatomical variation known as the nonrecurrent laryngeal nerve (NRLN) exists, where the right RLN arises directly from the main trunk of the vagus nerve in the upper neck, bypassing its usual course and entering the larynx near the lower pole of the thyroid. This variation is often associated with the right subclavian artery, which originates from the left side of the aortic arch. The incidence of this variation is higher on the right side than on the left [10].

Relevant data indicate that the incidence of NRLN ranges from 0.5% to 1.0% [11]. While the likelihood of this variation is relatively low, it remains a significant factor contributing to RLN injury. Failing to recognize the presence of an NRLN increases the risk of RLN damage during surgery [12, 13]. Therefore, a thorough preoperative assessment and understanding of the anatomical and physiological structure of the NRLN are crucial.

Principle of RLN monitoring

RLN monitoring technology operates by using a stimulation electrode to generate an electrical current of specific intensity. This electrical stimulation induces nerve impulses in the motor neurons, which are transmitted to the innervated muscles, causing muscle contractions and generating EMG signals. The monitoring electrode, in contact with the muscle, detects these EMG signals and transmits them back to the nerve-monitoring device for amplification and processing. The processed signals are displayed as an EMG trace and accompanied by an auditory alert, depending on the results [14].

The nerve monitoring system primarily consists of the monitoring device, stimulation equipment, recording equipment, and other related devices. A schematic diagram of the monitoring process is presented in **Figure 1**.

Monitoring device main unit

The main unit of the monitoring device is the core component of the nerve monitoring system. It generates electrical stimulation sig-

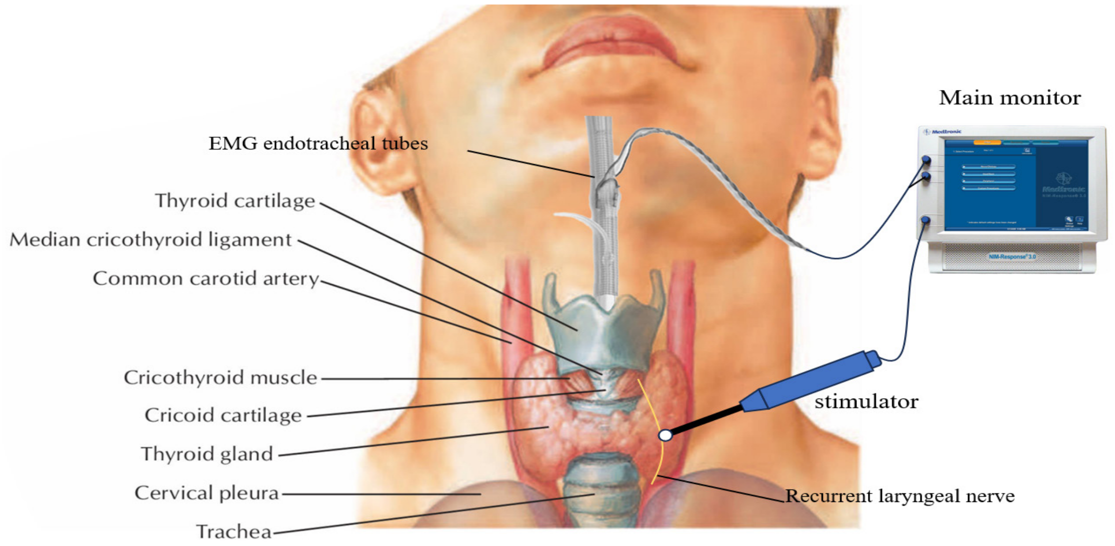

Figure 1. RLN monitoring. RLN, recurrent laryngeal nerve; EMG, electromyography.

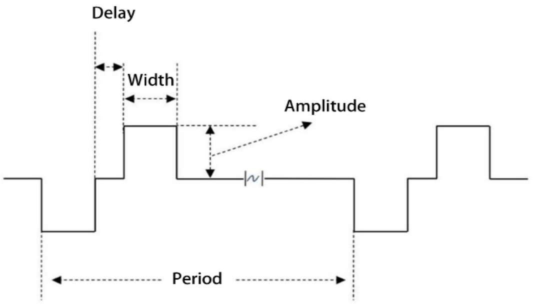

Figure 2. Pulse schematic diagram.

nals, processes EMG signals, issues alerts, and displays and stores information. Several parameters of the main unit can be adjusted during operation, including the event threshold, stimulation current intensity, stimulation frequency, and pulse width. The event threshold refers to the minimum amplitude that triggers a response from the system and can be set based on surgical requirements. Establishing an appropriate event threshold is crucial for optimizing early warning effectiveness in nerve injury detection.

The most widely used intraoperative nerve monitoring devices include the Medtronic series, Inimed series, and Dr. Langer Medical series.

(1) Medtronic Series: The Medtronic series includes three products: NIM-Response 3.0, NIM-Neuro 3.0, and NIM Vital.

NIM-Response 3.0 is specifically designed for RLN monitoring during thyroid and neck surgeries. It supports unilateral nerve monitoring and provides both audio and visual feedback on nerve function.

NIM-Neuro 3.0 offers multi-channel functionality, making it ideal for complex, high-risk surgeries.

NIM Vital (introduced in 2020) features a wireless design for both the patient interface and the console, making it portable and easy to position.

(2) Inimed Series: The Inimed series includes the C2 NerveMonitor and ISIS IOM System.

C2 NerveMonitor is designed for RLN monitoring, supporting bilateral stimulation and multi-channel recording.

ISIS IOM System is a comprehensive intraoperative nerve monitoring system that can monitor the RLN, facial nerve, and peripheral nerves simultaneously, making it suitable for complex surgeries, including neurosurgical applications.

(3) Dr. Langer Medical Series: The Dr. Langer Medical series includes the Neurosign 400 and Neurosign V4.

Neurosign 400 is specifically designed for RLN monitoring, allowing unilateral nerve monitoring with rapid nerve stimulation and feedback.

Neurosign V4 is a multifunctional nerve monitoring device with multi-channel capability, supporting various types of nerve monitoring.

Principle of electrical stimulation

The stimulating device, also known as the stimulation electrode, delivers electrical currents to depolarize motor nerve fibers, generating ac-

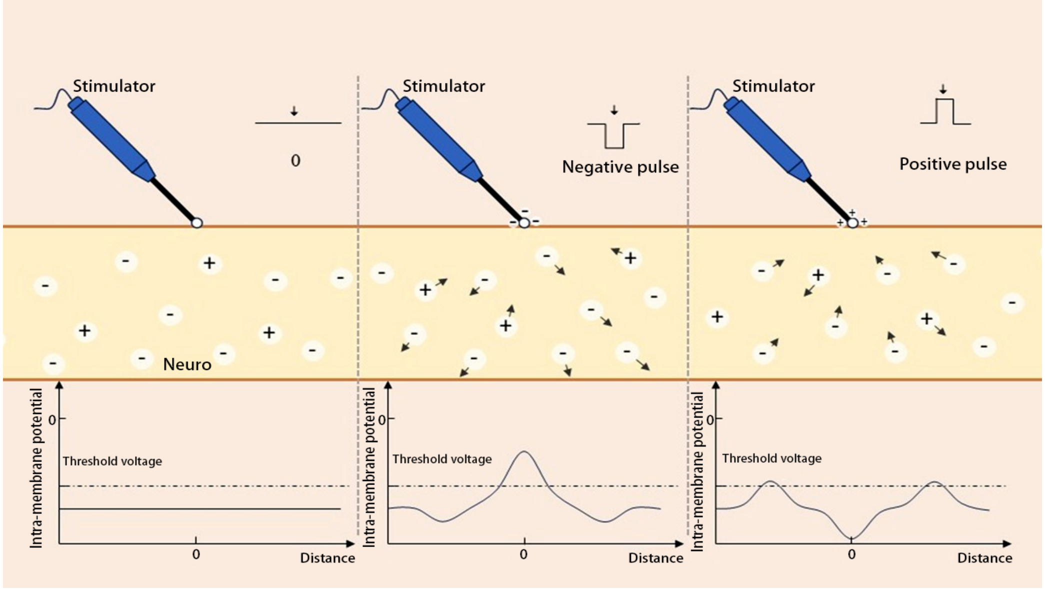

Figure 3. Schematic of a biphasic electrical stimulation pulse.

tion potentials that are transmitted to the vocal cord muscles innervated by the nerve. Stimulation electrodes come in two main types: monopolar and bipolar, with various probe designs, including spherical, needle-shaped, and hook-shaped electrodes. These electrodes differ in size, shape, electrode type, and contact form, allowing selection based on specific needs. Additionally, combining anatomical or endoscopic instruments with stimulation probes has gained attention for enhancing nerve monitoring precision during surgery. Wu et al. used ten different stimulation probes to stimulate the laryngeal nerves and monitor nerve function, demonstrating that monopolar electrodes, bipolar electrodes, and stimulating anatomical instruments are all effective in inducing nerve impulses, thus supporting RLN monitoring [15].

Electrical stimulation can be categorized into monopolar and bipolar modes based on the type of electrode used. In monopolar stimulation, the current is emitted from the stimulator, passes through tissue or nerve, and returns to the stimulation device via the return electrode plate. Due to the relatively large distance between the stimulator and the return electrode plate, current distribution in monopolar stimulation is more diffuse, making it suitable for locating the general course of nerves. In contrast, bipolar stimulation involves current flow between two probes placed a few millimeters apart, resulting in a more focused current distribution, which is particularly effective for precise nerve localization [15].

Electrical stimulation that induces nerve impulses can be generated using either a constant-voltage source or a constant-current source. The latter is preferred due to its stable current delivery, controllable stimulation effects, and reduced risk of overstimulation. Key parameters involved in electrical stimulation include pulse intensity, pulse width, pulse frequency, and stimulation waveform [16]. For RLN stimulation, the typical current range is 0-5 mA, with a pulse width of approximately 50-200 μs, a pulse interval of 100 μs, and a frequency of 1-4 Hz. These pulse parameters are illustrated in **Figure 2**.

Both positive and negative pulses can induce nerve impulses, though the mechanisms differ slightly. During negative pulse stimulation, the negative charge on the electrode causes a redistribution of charges on the axonal membrane [17]. Negative charges accumulate on the membrane’s exterior beneath the electrode, while positive charges inside the membrane move toward the electrode. This leads to depolarization beneath the electrode and hyperpolarization farther from it. When the membrane potential reaches the threshold voltage, an action potential is triggered. Positive pulses induce the opposite effect: positive charges accumulate on the electrode, moving negative charges inside the membrane toward the electrode, leading to depolarization further from the electrode and hyperpolarization near it. When the membrane potential reaches threshold, an action potential is triggered. The action potentials induced by both positive and negative pulses are illustrated in **Figure 3**.

Regarding stimulation waveforms, the main types are monophasic pulse, symmetric biphasic pulse, and asymmetric biphasic pulse [16]. Domestic researchers have verified various

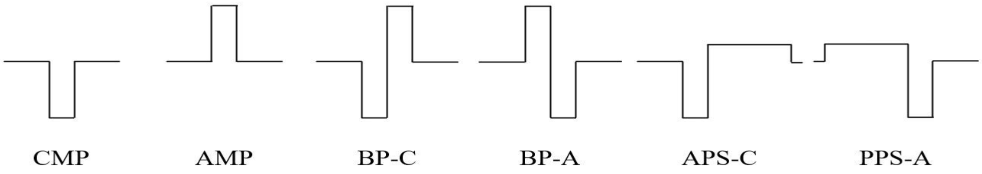

Figure 4. Schematic of stimulation waveform. CMP, monophasic pulse; AMP, anodic monophasic pulse; BP-C, cathodic first charge-balanced biphasic pulse; BP-A, anodic first charge-balanced biphasic pulse; APS-C, cathodic first charge-balanced anterior pseudomonophasic pulse; PPS-A, anodic first charge-balanced posterior pseudomonophasic pulse.

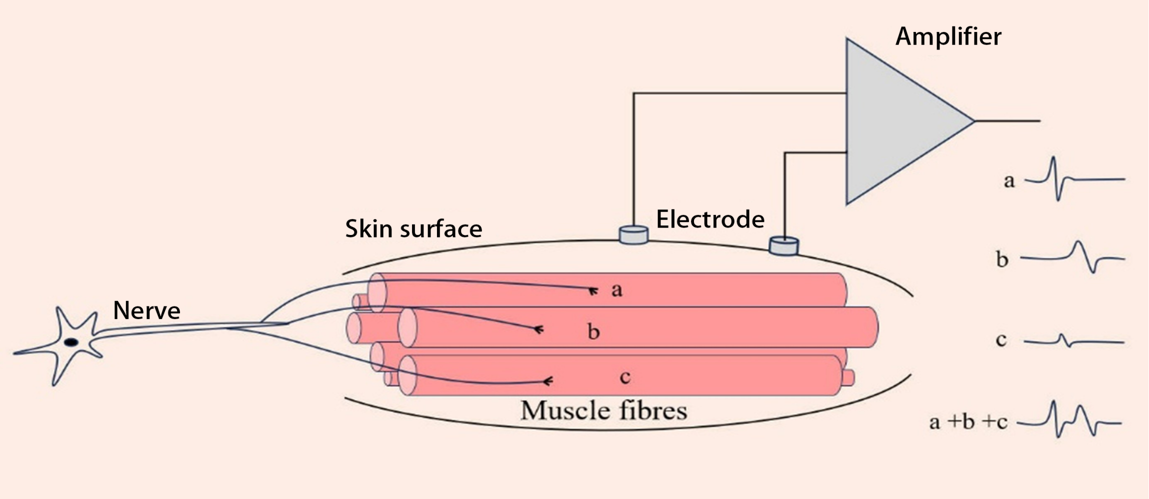

Figure 5. Schematic diagram of muscle fiber formation of EMG signal. EMG, electromyography.

pulse signals, including the Cathodic Monophasic Pulse, Anodic Monophasic Pulse, Cathodic First Charge Balanced Biphasic Pulse, Anodic First Charge Balanced Biphasic Pulse, Cathodic First Charge Balanced Anterior Pseudomonophasic Pulse, and Anodic First Charge Balanced Posterior Pseudomonophasic Pulse. The excitation induced by these waveforms, from largest to smallest, is as follows: Cathodic Monophasic Pulse, Cathodic First Charge Balanced Anterior Pseudomonophasic Pulse, Cathodic First Charge Balanced Biphasic Pulse, Anodic First Charge Balanced Posterior Pseudomonophasic Pulse, Anodic First Charge Balanced Biphasic Pulse, and Anodic Monophasic Pulse. These waveforms are illustrated in **Figure 4**. For RLN stimulation, biphasic pulse stimulation is generally preferred to avoid charge imbalance on the nerve and prevent electrode corrosion. The first phase of a biphasic pulse is a negative pulse to activate neurons, while the second phase is a positive pulse to balance the charge.

Principle of EMG signal acquisition

The purpose of the recording device is to capture EMG signals from muscles innervated by the nerve. Neuronal discharge activates numerous muscle fibers, and the cumulative activity of these fibers generates the EMG signal. As the force exerted by the body increases, more muscle fibers are recruited, resulting in a corresponding increase in the amplitude of the EMG signal [18]. The EMG signal is shown in **Figure 5**. By analyzing the waveform, amplitude, and latency of the EMG signal, nerve damage can be assessed. A detailed description of the EMG signal is provided in **Figure 6**.

The EMG signal can be captured using surface electrodes on the monitoring catheter in direct contact with the vocal cords or by inserting a needle electrode into the lower and lateral parts of the thyroid cartilage's anterior horn. Zhao et al. compared three types of recording electrodes using pigs: monitoring catheter surface electrodes, thyroid cartilage adhesive electrodes, and thyroid cartilage needle electrodes [19]. Their findings indicated that the monitoring performance of all three electrodes was nearly identical. However, non-invasive, indwelling monitoring via catheter electrodes is more commonly used in clinical practice [20].

To visualize the EMG signal, it is important to recognize that EMG signals are weak bioelectrical signals with small amplitudes (1 mV to 10 mV) and a frequency range of 0-500 Hz. These signals are highly susceptible to external interference, such as power-line noise,

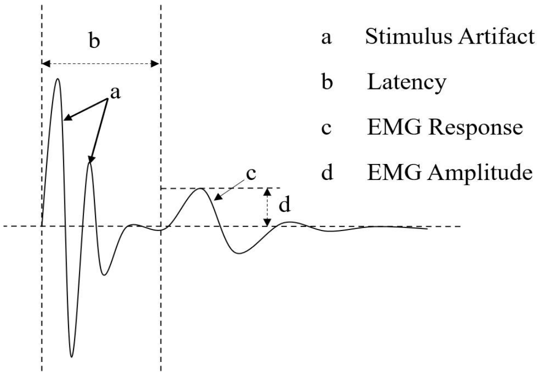

Figure 6. Schematic diagram of EMG signal description. EMG, electromyography.

equipment-generated noise, and movement artifacts. Therefore, the raw EMG signal must be amplified several thousand times and filtered to remove unwanted noise [18]. In the circuit, an instrumentation amplifier is used with a main amplifier to amplify the EMG signal. The instrumentation amplifier provides a high common-mode rejection ratio (CMRR), initially amplifying the signal by several tens of times. The main amplifier further amplifies the signal by tens to hundreds of times. A filtering circuit, including high-pass and low-pass filters, isolates the primary frequency range of the EMG signal. A notch filter is employed to eliminate power-line interference. Finally, the processed EMG data is converted into a digital signal and processed by a microcontroller [21]. The flowchart of the EMG signal acquisition process is shown in **Figure 7**. Other devices, such as line connection devices, storage equipment, and printing devices, are also used.

Current research status of RLN monitoring technology

RLN monitoring technology has been widely adopted worldwide, and decades of development have led to continuous innovation in this field. Current advancements in RLN monitoring technology focus on four main areas: the stimulation end, signal acquisition, monitoring instrument software, and application methods.

Innovation in the stimulation end involves integrating anatomical instruments with stimulation probes, resulting in devices like the stimulating dissector. This tool allows surgeons to seamlessly switch between anatomical instruments and stimulation probes, improving convenience and efficiency [22-24]. The most common signal acquisition method is using an endotracheal tube with surface electrodes, which is non-invasive and easy to use. Recent innovations include the thyroid cartilage needle electrode, which indirectly contacts the effector muscles, offering more precise signal acquisition with enhanced sensitivity [19, 25].

Innovations in monitoring instrument software aim to improve signal sensitivity, automate waveform analysis, enhance anti-interference capabilities, and provide user-friendly features.

Regarding application methods, two key innovations have emerged. The first is minimally invasive thyroidectomy assisted by endoscopy, using endoscopic forceps equipped with nerve monitoring capabilities. This procedure can be performed via axillary or bilateral axillary-breast approaches or through natural orifice surgery. Minimally invasive thyroidectomy offers high cosmetic satisfaction and comparable surgical outcomes and complication rates to traditional thyroidectomy [26, 27]. The second innovation is robot-assisted thyroidectomy, which leverages the precision and flexibility of robotic systems to overcome the limitations of traditional and endoscopic thyroidectomy, offering new directions for surgical innovation [28, 29].

Monitoring process

The monitoring process is complex and requires collaboration among various professionals, including the surgeon, anesthesiologist, technical experts, and neuro-monitoring staff. Each plays a specific role and contributes to the process. If neuro-monitoring personnel lack proper training or if neuro-monitoring procedures are not standardized, it can lead to inaccurate neurophysiological data, potentially misleading the surgeon. Therefore, adherence to standardized neuro-monitoring protocols, accurate analysis of abnormal conditions, and the identification of appropriate patient populations are essential for maximizing the benefits of this technique.

Steps of RLN monitoring technique

To ensure successful RLN monitoring, standardized operational procedures must be followed. The international guidelines for RLN monitoring, published in 2011 and 2013, outline the steps for intraoperative nerve monitoring, including preoperative laryngoscopy, preoperative vagus nerve identification, postoperative vagus nerve detection, and postoperative laryngoscopy [20, 30].

The Thyroid Surgery Committee of the Chinese Medical Association's Surgical Physician Branch has published clinical guidelines for intraoperative nerve monitoring during thyroid and parathyroid surgeries in 2013, 2017, 2019,

Table 1. RLN monitoring steps

Abbreviations	Specific steps
L1	Preoperative Laryngeal Examination
V1	Preoperative Vagus Nerve Detection
R1	After precisely locating the RLN, detect the RLN
S1	Pre-Thyroid Upper Pole Vascular Handling: Detection of the External Branch of the Superior Laryngeal Nerve
S2	Post-Thyroid Upper Pole Vascular Handling: Detection of the External Branch of the Superior Laryngeal Nerve
R2	Postoperative Detection of the RLN
V2	Postoperative Detection of the vagus nerve
L2	Postoperative Laryngeal Examination

Note: RLN, Recurrent Laryngeal Nerve.

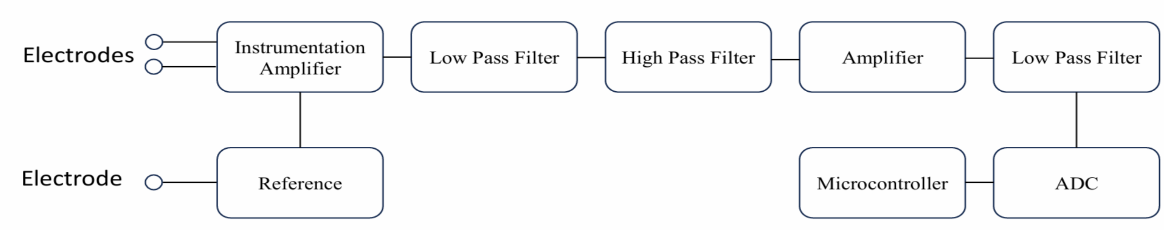

Figure 7. EMG signal acquisition. ADC, analog-to-digital converter; EMG, electromyography.

and 2023. These guidelines define standardized procedures for nerve monitoring and offer recommendations.

Since the release of the first Chinese guidelines in 2013, the procedures for RLN monitoring have gained widespread recognition in the medical community. The monitoring process has evolved from an initial six-step method to an eight-step method (**Table 1**). These steps include: preoperative laryngeal examination (L1), preoperative vagus nerve detection (V1), RLN detection (R1), detection of the external branch of the superior laryngeal nerve before handling the thyroid upper pole vessel (S1), detection of the external branch of the superior laryngeal nerve after handling the thyroid upper pole vessel (S2), postoperative RLN detection (R2), postoperative vagus nerve detection (V2), and postoperative laryngeal examination (L2).

By comparing signals before and after surgery, the function of the nerve can be assessed, providing valuable information for subsequent diagnosis and treatment.

Analysis and handling of abnormal EMG signals

Abnormal EMG signals are characterized by a significant decrease in the amplitude of the EMG signal during surgery, compared to the normal signals obtained preoperatively. In a dry environment, with an electrical stimulation intensity of 1-2 mV, if the amplitude of the EMG signal drops below 100 μV and there is no laryngeal or glottic twitching, it is considered as the loss of the EMG signal [31]. Abnormal EMG signals may be caused by issues with the monitoring system or nerve damage. When abnormal signals are detected, it is crucial to identify the cause quickly and take appropriate measures to minimize RLN damage and adjust the surgical plan if necessary.

During surgery, the first step when abnormal EMG signals are detected is for the surgeon to assess the laryngeal spasm response. This involves stimulating the ipsilateral vagus nerve and observing the laryngeal muscle tremor. The surgeon should palpate the cricothyroid muscle at the posterior aspect of the cricoid cartilage to monitor for muscle contraction. If a laryngeal spasm response is observed, it indicates that the stimulation system and neural function are intact, suggesting the abnormal signal may be due to issues with the recording equipment. The most common problem with recording equipment is electrode misplacement, which can occur due to catheter displacement, improper depth placement, or poor contact. In such cases, the monitoring catheter should be repositioned.

It is also important to check for poor contact with the grounding electrode. Sweat accumulation may cause the grounding electrode to detach or shift. If no laryngeal spasm response is observed, the issue may lie with the stimulation system. The first step is to verify whether the stimulation current is sufficient. If the current is abnormal, it could be due to a malfunction of the stimulation electrode or incorrect stimulation channel settings. In this case, the stimulation electrode should be replaced or the stimulation channel adjusted. If the stimulation current is normal, the issue could be caused by excess fluid in the surgical field, leading to current dispersion. In such cases, the surgical field should be dried.

Neural injury analysis and management

If the initial EMG signal is normal and a sufficiently strong stimulation current is applied to the nerve, but the EMG signal becomes abnormal or disappears without any laryngeal spasm response under laryngoscopy, a thorough review of the lost EMG signal is required. If no issues are found with the monitoring system, the surgeon should strongly suspect nerve injury. Neural injuries detected through IONM can be categorized into two types. Type I injury, also known as segmental injury, refers to the identification of a specific point or site of injury in the RLN. This type of injury is most commonly caused by excessive traction, clamping, or thermal injury, with traction being the most frequent cause [4, 32]. Type II injury, or complete injury, occurs when no EMG signals are detected in both the RLN and the ipsilateral vagus nerve, but signals are present in the contralateral RLN and vagus nerve. In Type II injury, no specific point or segment of injury can be identified, and the underlying mechanism remains unclear.

Traction-induced RLN injury is the most common form, with the EMG signal gradually decreasing in proportion to the extent of traction. If detected early and addressed promptly, the EMG signal may recover. If the RLN signal drops to 50% or less of its normal amplitude, this serves as an early warning of potential nerve injury [33]. In such cases, surgery should be paused, and a 20-30-minute observation period should be allowed to assess whether the signal recovers, while the possible causes are analyzed. If the EMG signal recovers, surgery can resume, but extra caution should be taken to avoid further injury. If the EMG signal does not recover, it may be necessary to adjust the surgical plan accordingly [34].

Summary

IONM technology provides an effective means of assessing RLN injury during surgery, offering valuable support to surgeons. However, challenges remain in the application of RLN monitoring technology: monitoring personnel must receive specialized training, surgeons must be skilled in standardized procedures, and they must be able to troubleshoot abnormal signals effectively. IONM technology requires rapid and precise physiological signal acquisition and response, imposing stringent demands on both hardware and software. To meet these challenges, nerve monitoring devices must improve sensitivity, automate waveform analysis, and enhance anti-interference capabilities, minimizing the risk of intraoperative nerve injury.

As technology continues to advance, nerve monitoring equipment is expected to evolve toward greater sensitivity, faster and more accurate waveform analysis, and enhanced user-friendliness. Moreover, minimally invasive thyroidectomy and robot-assisted thyroidectomy are likely to be key areas of focus for the future development of thyroid surgery.

Author contributions: Yong Wang was responsible for collecting data, writing the paper, revising the content, and proofreading the paper. Yu Zhou was responsible for providing direction for the paper and guiding the writing.

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